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THE NATURAL HISTORY OF CARCINOMA OF THE LUNG

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THE NATURAL HISTORY OF CARCINOMA OF THE LUNG

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IN THE MAJORITY of instances, early diagnosis and ablation of cancer will yield the greatest number of cures. Since the most radical operation practicable is currently used for cancer of the lung, earlier diagnosis should improve the present 3 to 6 per cent cure rate.

Use of clinical diagnostic methods such as bronchoscopy, cytology, scalene biopsy, and thoracotomy have increased in recent years and have helped to make earlier definitive diagnosis. However, a significant change on a roentgenogram of the chest frequently is the first positive finding and often precedes clinical symptoms. The principal objective of this study has been to gain new information about these early changes and, where possible, to observe the alteration in such x-ray shadows with the passage of time. To this end, all roentgenograms obtainable on proved cases of pulmonary cancer have been collected and studied.

METHOD

Over 400 cases of pulmonary cancer seen in this hospital have been reviewed. This report covers 360 proved cases, the majority having been diagnosed within the past 15 years. Records were abstracted and information was solicited from surviving patients, families, physicians, hospitals, and other institutions where radiographs may have been taken. Any past radiographs available were gathered and reviewed in conjunction with later films made at the time of the diagnosis of the patient's carcinoma. All films were studied in joint session by the authors. Where there was any question of the presence of an abnormal shadow, the opinion of two unbiased senior radiologists was obtained.

RESULTS

While the radiographic study of these cases has been the prime aim of the project, certain ancillary statistical information is included for general interest with no further elaboration. Tables I through VI list statistics relating to age, sex, occupation, smoking habits, symptoms, diagnostic methods, and cell type.

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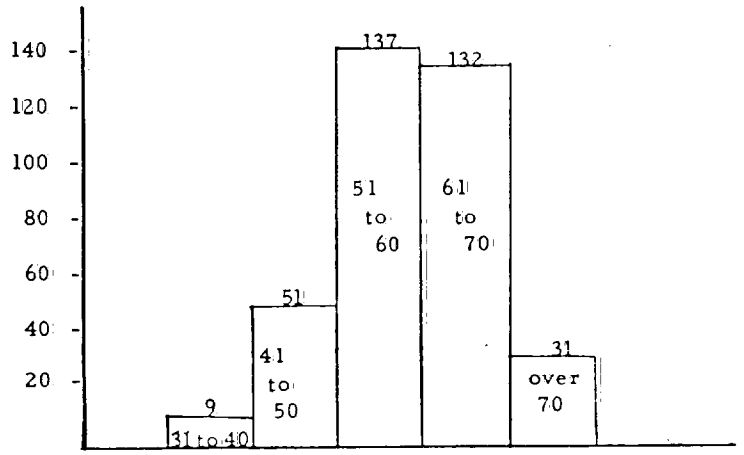
TABLE I. SEX AND AGE DISTRIBUTION IN 360 CASES OF LUNG CANCER

	NUMBER	PER CENT	AVERAGE AGE
Male	313	87	59.4
Female	47	13	56.2
Total	360	100	58.9



Age distribution of patients

TABLE II. OCCUPATIONS IN 360 CASES OF LUNG CANCER*

OCCUPATION	NUMBER	PER CENT
White collar worker	82	22.8
Housewife	37	10.3
Not known	34	9.4
Hazardous dust exposure	29	8.1
Truckdrivers and mechanics	26	7.2
Laborers	18	5.0
Carpenters	17	4.7
Farmers	15	4.2
Machinists	14	3.9
Painters	12	3.3
Railroad yard and engine workers	9	2.5
Restaurant workers	8	2.2
Tailors	8	2.2
Janitors	6	1.7
Plumbers	5	1.4
Pressers	5	1.4
Garbage collectors	4	1.1
Bartenders	3	0.8
Barbers	3	0.8
Gardeners	3	0.8
Laundry workers	3	0.8
Porters	3	0.8
Stationary engineers	3	0.8
Basket weavers	2	0.6
Firemen	2	0.6
Grocers	2	0.6
Policemen	2	0.6
Printers	2	0.6
Miscellaneous (1 each)	5	0.3

*Total figure reflects multiple occupations.

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TABLE III. SMOKING HABITS IN 360 CASES OF LUNG CANCER

	WOMEN		MEN		TOTAL	
	NO.	%	NO.	%	NO.	%
No information	18	38	129	41	147	41
Nonsmokers	18	38	7	2	25	7
Group A smokers*	6	13	92	30	98	27
Group B smokers†	5	11	85	27	90	25
Total	47	100	313	100	360	100

	MEN EXPOSED TO DUST‡		MEN EXPOSED TO COMBUSTION FUMES		TOTAL FOR SMALLER GROUP PAST 4 YEARS§	
	NO.	%	NO.	%	NO.	%
No information	9	31	6	23	39	24
Nonsmokers	0	—	0	—	12	7
Group A smokers	7	24	4	15	56	35
Group B smokers	13	45	16	62	55	34
Total	29	100	26	100	162	100

*Smokers of less than 1 package per day.
†Smokers of 1 package or more per day for 20 plus years.
‡For example, dusts with a potential for producing pneumoconiosis.
§Reflects better recorded information in more recent years.

TABLE IV. OCCURRENCE OF SYMPTOMS IN 360 CASES OF LUNG CANCER

FIRST SYMPTOM			LATER SYMPTOMS		
	NO.	%		NO.	%
1. Cough	194	54	1. Sputum	214	60
2. Chest pain	38	11	2. Chest pain	151	42
3. Weight loss	30	8	3. Hemoptysis	130	36
4. Dyspnea	20	6	4. Dyspnea	109	30
5. No symptoms	19	5	5. Weight loss	89	25
6. Fatigue	17	5	6. Cough	85	23
7. Bone pain	12	3	7. Wheeze	37	10
8. Pleuritic pain	7	2	8. Pleuritic pain	27	8
9. Nerve disorder	7	2	9. Hoarseness	23	6
10. Hemoptysis	5	1	10. Nerve disorder	21	6
11. Hoarseness	4	1			
12. Mass in neck	3	1			
13. Misc. (1 each)	4	1			

TABLE V. DIAGNOSTIC PROCEDURES IN 360 CASES OF CARCINOMA OF THE LUNG

PROCEDURE	NUMBER	PER CENT OF PROCEDURES	PER CENT OF SERIES
Bronchoscopy			
Total examinations	230	100	64
Abnormal appearance	191	83	53
Positive biopsy	99	43	28
Negative biopsy	39	17	11
Scalene Biopsy			
Total examinations	70	100	19
Positive biopsy	46	66	13
Negative biopsy	24	34	7
Papanicolaou Smear			
Total examinations	84	100	23
Positive	63	75	17
Negative	21	25	6
Thoracotomy			
Total operations	150	100	42
Pneumonectomy	60	40	17
Lobectomy	18	12	5
Nonresectable	72	48	20

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TABLE VI. CELL TYPE IN 360 CASES OF CARCINOMA OF THE LUNG

CELL TYPE	MEN	WOMEN	TOTAL	PER CENT
Epidermoid	137	9	146	40
Undifferentiated epidermoid	127	16	143	40
Adenocarcinoma	16	17	33	9
Oat cell	17	0	17	5
Not classified	6	3	9	3
No section (gross appearance; cytology)	10	2	12	3

Table VII is a clinical analysis of 10 patients surviving 5 years or more, an incidence of 2.8 per cent of the total group and 3.1 per cent of the cases seen during the 15-year period in which these survivors were diagnosed.

Table VIII indicates the average interval from the first symptom to clinical diagnosis, to pathologic diagnosis, and to death in varying numbers of patients.

Of major concern in this study is the information tabulated in Tables IX and X. These indicate the average interval elapsing between the earliest radiographic evidence of the individual's cancer and the clinical diagnosis (Table IX) and the pathologic diagnosis (Table X). In each case, this is averaged for four categories: (1) all cases; (2) excluding patients in which the interval between the earliest radiographic evidence and diagnosis was zero; (3) excluding patients in which this interval was less than 3 months; and (4) excluding all cases in which this interval was less than 6 months. Because of the nature of the shadows seen in x-ray studies at the time of diagnosis, it is highly probable that some abnormality would have been present if films had been taken at any point during the 6 months or year prior to diagnosis. Therefore, the more significant is the last group. Rigler and his group have been interested in the duration of pulmonary cancer for some time and have brought out this point.[3, 4]

Radiographic Findings.—As previously stated, the major interest in this project has centered around a study of the early radiographic evidences of carcinoma of the lung. In reviewing all earlier films, changes have been sought which could be correlated with the eventual, more gross evidence, of the neoplasm. The types of change seen and their frequency are recorded in Table XI.

1. *Obstructive pneumonitis:* One of the commonest morphologic manifestations of lung cancer, found in 36 per cent of this series, is the encirclement of, or growth into, a bronchus by the neoplasm. This produces a partial obstruction and consequent poor drainage distally. Radiographically, the tumor itself may not be seen while the secondary changes of obstructive pneumonitis are quite common. The term implies a subacute or chronic infiltration with additional evidence of decreased lung volume locally. An illustration of this is given in Figs. 1-4. The inflammatory process is indicated by the heavy linear infiltration at the left base and the partial atelectasis by the elevated diaphragm.

2. *Parenchymal mass:* Twenty-two per cent of the cases had radiographs revealing the direct shadow produced by the more peripherally situated tumor. Illustrations of this are found in Fig. 5, representing a slowly growing lesion, and in Figs. 6-9, representing a rapidly progressive neoplasm. It will be noted

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TABLE VII. CLINICAL ANALYSIS OF 10 CASES OF LUNG CANCER SURVIVING 5 OR MORE YEARS AFTER OPERATION

CASE	SEX	INTERVAL FIRST SYMPTOM TO DIAGNOSIS (MO.)	INTERVAL FIRST X RAY CHANGE TO DIAGNOSIS	OPERATION	CELL TYPE	CLINICAL STATUS
B. C.	F	1	1 week	Pneumonectomy, Rt., Oct. 1942	Epidermoid	Moderately decreased pulmonary function
H. C.	M	3	5 months	Pneumonectomy, Rt., Dec. 1950	Epidermoid	Pulmonary status good
J. C.	M	4	2 months	Pneumonectomy, Lt., Dec. 1948	Epidermoid	Died 6 years postop. of unrelated disease
E. E.	M	11	2 months	Pneumonectomy, Rt., Oct. 1951	Epidermoid	Well
C. G.	M	5	4 months	Pneumonectomy, Rt., Sept. 1952	Epidermoid	Well with slightly decreased pulmonary function
L. K.	F	No symptoms	31 months	Lobectomy, Rt., Nov. 1950	Adenocarcinoma	Well; see Fig. 5
J. L.	M	2	1 month	Pneumonectomy, Lt., Jan. 1943	Epidermoid	Moderately decreased pulmonary function
P. L.	M	2	None	Pneumonectomy, Lt., Feb. 1950	Epidermoid	Psychotic; no evidence of recurrence
A. T.	M	16	None	Pneumonectomy, Rt., Apr. 1951	Epidermoid	Died 5½ years postop. of unrelated disease
S. W.	M	5	None	Pneumonectomy, Lt., June 1952	Epidermoid	Died 5 years postop. with probable metastases

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TABLE VIII. AVERAGE INTERVAL BETWEEN FIRST CLINICAL SYMPTOM AND CLINICAL DIAGNOSIS, PATHOLOGIC DIAGNOSIS, AND DEATH IN 359* CASES OF LUNG CANCER

	NO. OF PATIENTS	AVERAGE INTERVAL (MO.)	EXTREMES OF INTERVAL
Interval between first symptom and clinical diagnosis	359	6.8	0 to 60 mo.
Interval between first symptom and pathologic diagnosis	359	7.8	0 to 60 mo.
Interval between first symptom and death	305	13.8	2 wk. to 104 mo.

*One case had no recorded clinical history.

TABLE IX. AVERAGE INTERVAL BETWEEN THE EARLIEST RADIOGRAPHIC EVIDENCE OF LUNG CANCER AND THE CLINICAL DIAGNOSIS IN 350* CASES

	NO. OF PATIENTS	AVERAGE INTERVAL (MO.)
All cases	350	4.0
Excluding 153 cases in which earliest evidence coincides with the clinical diagnosis	197 (56%)	7.1
Excluding 238 cases in which the earliest evidence was less than 3 months from clinical diagnosis	112 (32%)	11.8
Excluding 276 cases in which the earliest evidence was less than 6 months from clinical diagnosis	74 (21%)	15.9

*Ten cases of series had no available x-ray studies for review.

TABLE X. AVERAGE INTERVAL BETWEEN THE EARLIEST RADIOGRAPHIC EVIDENCE OF LUNG CANCER AND THE PATHOLOGIC DIAGNOSIS IN 350* CASES

	NO. OF PATIENTS	AVERAGE INTERVAL (MO.)
All cases	350	5.1
Excluding 81 cases in which the earliest evidence coincides with pathologic diagnosis	269 (77%)	6.1
Excluding 215 cases in which the earliest evidence was less than 3 months from the pathologic diagnosis	135 (39%)	12.2
Excluding 238 cases in which the earliest evidence was less than 6 months from the pathologic diagnosis	92 (26%)	16.1

*Ten cases of the series had no available radiographs for review.

that, of the ten parenchymal lesions a centimeter or smaller in size, none was associated with any other radiographic change. However, half of those over a centimeter in size were associated with other abnormalities such as hilar enlargement, mediastinal nodes or pleural effusion, an indication of extension of disease. This is a strong argument for early excision of any questionable peripheral lesion.

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3. *Hilar nodule:* In 20 per cent of this series, a subtle increase in size of the hilar shadow was found, frequently best observed by comparison with a previous normal x-ray study. In the majority of instances this change represented the direct evidence of the neoplasm (Figs. 10 and 11).

4. *Hilar mass:* Almost equal in frequency of presenting radiographic shadows was the much more obvious massive enlargement of the hilar shadow, a change making diagnosis much easier and prognosis correspondingly poor.

TABLE XI. TYPES OF EARLY RADIOGRAPHIC ABNORMALITIES FOUND IN 350* CASES PROVED TO BE LUNG CANCER

RADIOGRAPHIC FINDING	TOTAL		FOUND ALONE		WITH 1 OTHER ABNORMALITY		WITH 2 OTHER ABNORMALITIES	
	NO.	%	NO.	%	NO.	%	NO.	%
Obstructive pneumonitis	129	36.8	60	16.7	56	15.5	13	3.6
Parenchymal mass	77	21.4	45	12.5	24	6.7	8	2.2
Over 1 cm. in size	67	18.6	35	9.7	24	6.7	8	2.2
1 cm. or less in size	10	2.8	10	2.8	0		0	
Hilar nodularity	72	20.0	17	4.7	47	13.1	8	2.2
Hilar mass	69	19.4	35	9.7	25	6.9	9	2.5
Atelectasis	53	14.8	27	7.5	26	7.2	0	
Mediastinal nodes or mass	32	8.9	6	1.7	19	5.3	9	2.5
Pleural effusion	30	8.3	4	1.1	20	5.6	7	1.9
Parenchymal fibrous infiltrate	11	3.1	9	2.5	2	0.6	0	
Perihilar infiltrate	10	2.8	8	2.2	2	0.6	0	
Parenchymal mass with breakdown	8	2.2	6	1.7	2	0.6	0	
Obstructive emphysema	7	1.9	1	0.3	6	1.7	0	
Lung infection with abcess	5	1.4	3	0.8	2	0.6	0	
Diffuse parenchymal tumor	2	0.6	1	0.3	1	0.3	0	

*Ten cases of total series had no available radiographs for review.

5. *Atelectasis:* Atelectasis was found in 15 per cent of the patients. Since all but one of these have died, complete obstruction of a bronchus from a tumor is considered by the authors as a poor prognostic sign. Figs. 12 and 13 illustrate a patient presenting with left lower lobe atelectasis which was thought to be an aortic aneurysm.

6. *Parenchymal infiltrative density:* An example of a carcinoma beginning as a vague fibrous infiltration is shown in Figs. 14 and 15. This change is found with the same frequency as the small parenchymal nodule but is more often confused with old infection.

7. *Miscellaneous:* Less frequent presenting radiographic changes such as fluid, emphysema, abscess, etc., are listed in Table XI.

DISCUSSION

An average interval of almost 7 months between the first symptom and the clinical diagnosis emphasizes the continued need for improvement in cancer education of the public and the medical profession.

Again, referring to Tables IX and X, an interval between abnormal x-ray shadows and diagnosis of 4 months for all cases, or almost 16 months for a

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Fig. 1.

Fig. 2.

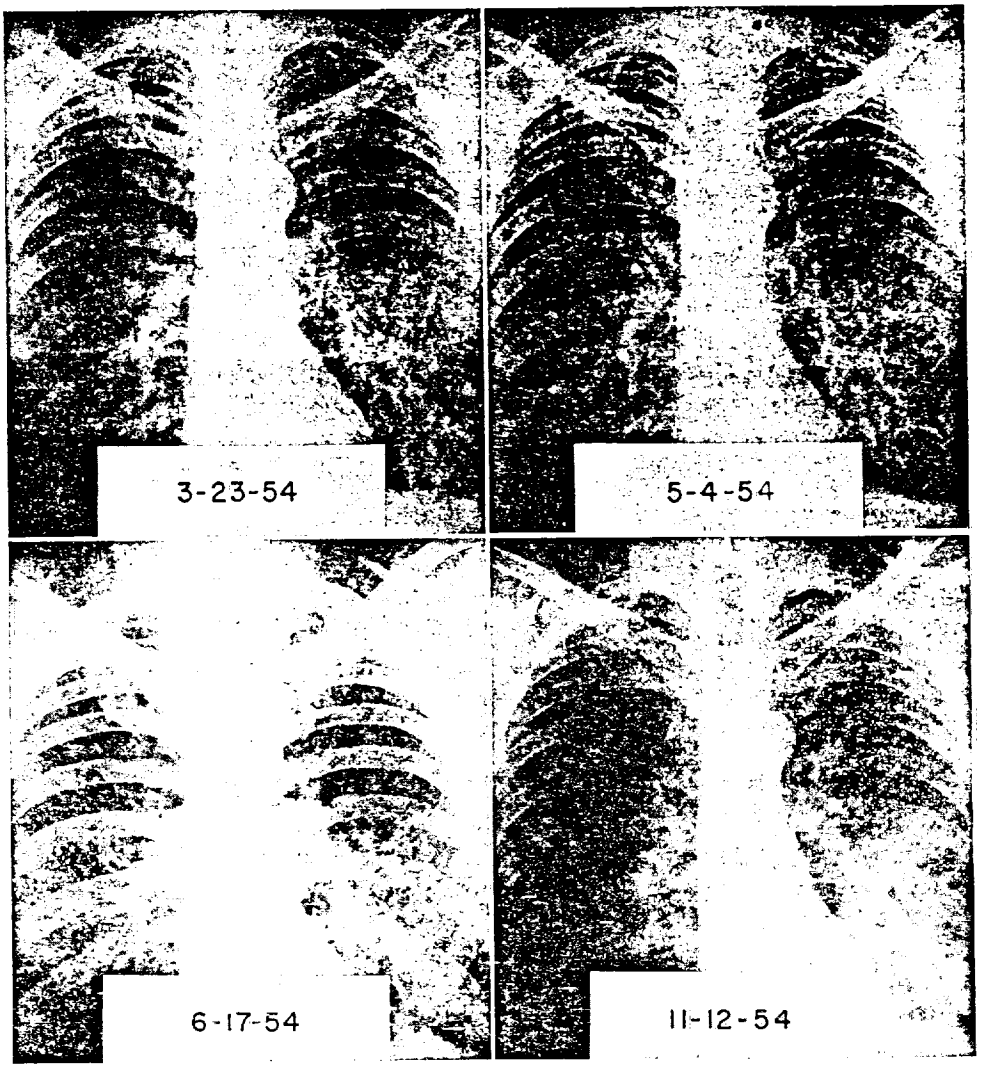

Fig. 3.

Fig. 4.

Figs. 1-4.—S. D., SMH No. 65317. A 47-year-old former truck driver with cough for the past 20 years which was worse following a bout of pneumonia 3½ years before. He had had frequent bouts of bronchitis. Patient was followed with x-ray studies which were interpreted as chronic pneumonitis for 7½ months during which time he lost 16 pounds in weight. Bronchoscopy and left pneumonectomy on 11/19/54 revealed epidermoid carcinoma. Patient is alive and well as of December, 1957. Progressive obstructive pneumonitis in the left lower lung field is seen in Figs. 1, 2, 3, and 4.

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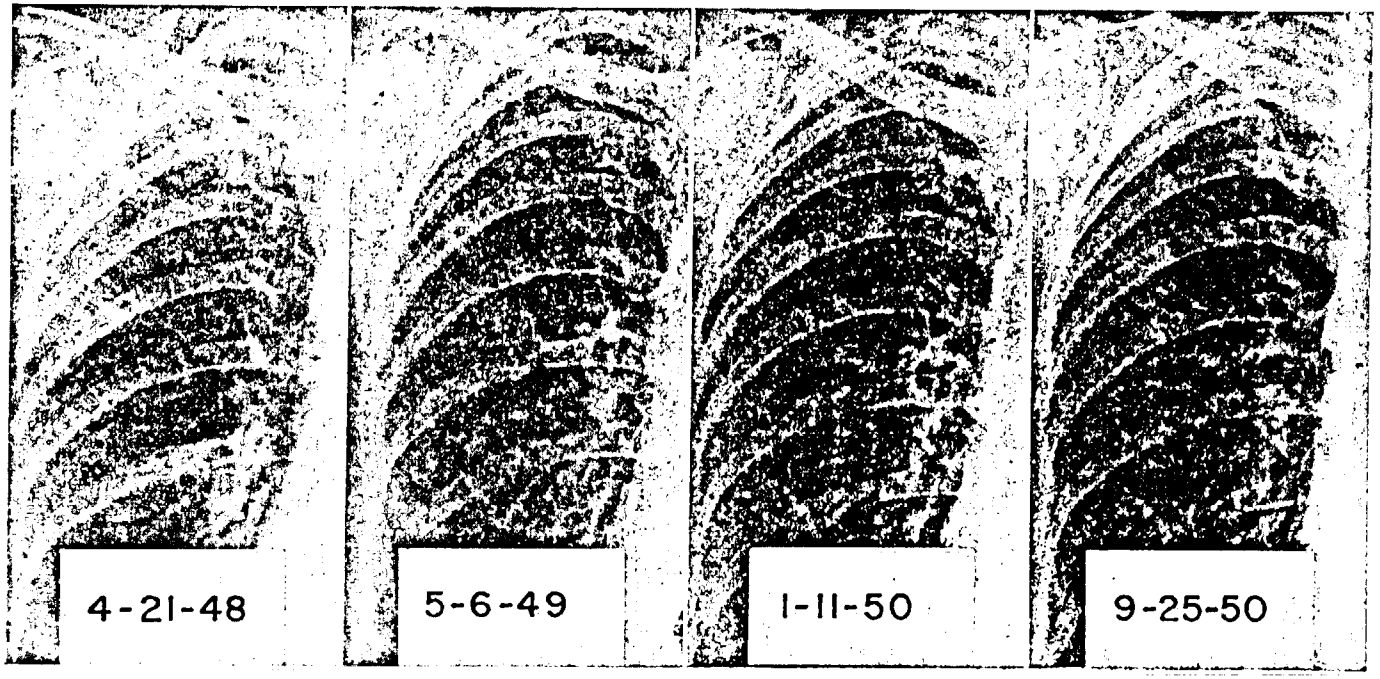

Fig. 5.—L. K., SMH No. 320241. A 53-year-old woman without symptoms. The lesion overlying the third rib anteriorly on film dated 4/21/48 was found on routine annual survey. Growth of the lesion on subsequent films over a period of 2½ years is evident, delay being primarily a medical responsibility. On 11/16/56 a right upper lobectomy revealed an adenocarcinoma. Patient is alive and well as of December, 1957.

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Fig. 6.

Fig. 7.

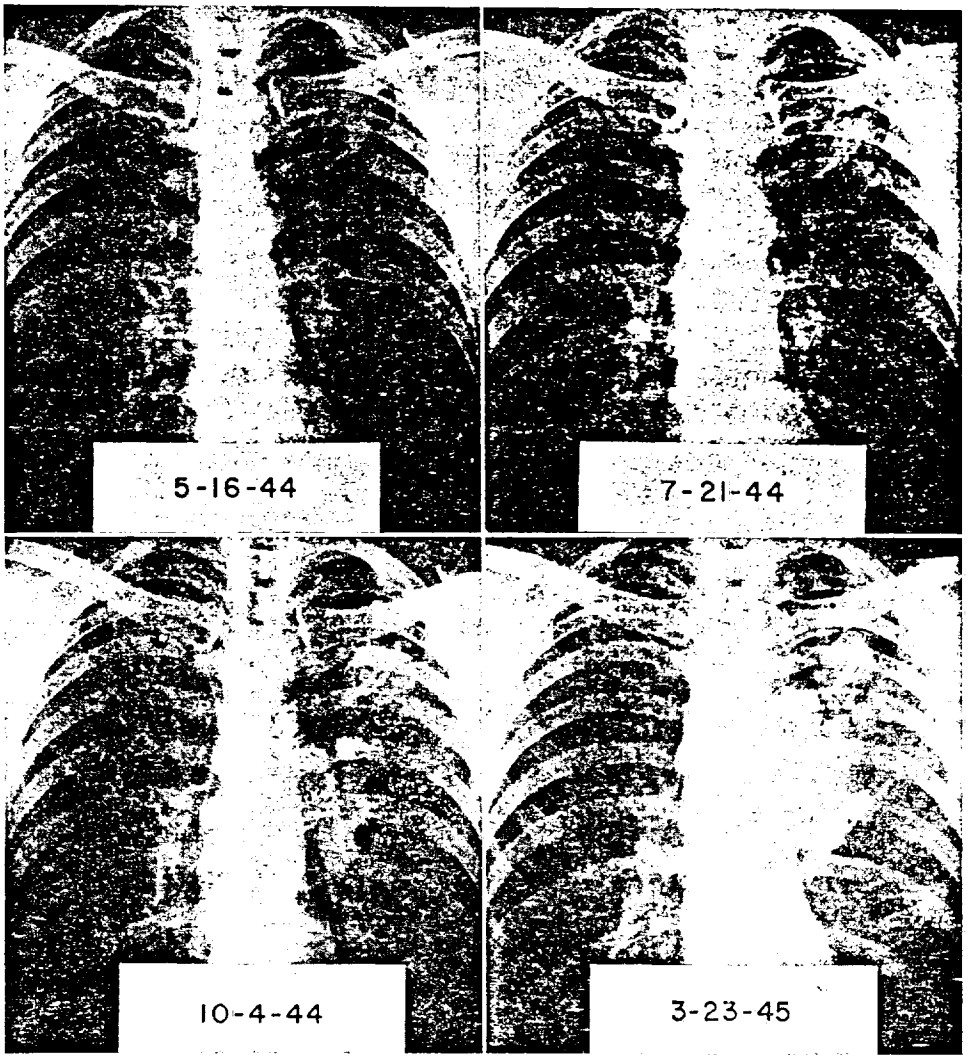

Fig. 8.

Fig. 9.

Figs. 6-9.—A. H., SMH No. 230290. A 53-year-old male worker in a tuberculosis sanitarium with negative yearly chest roentgenograms from 1937. His first symptom of hoarseness did not occur until 3 months after the film illustrated in Fig. 6. This was followed as tuberculosis without bacteriologic proof. In contrast to the case in Fig. 5, note the rapid growth of the lesion in the left upper lung field; also note rapid enlargement of the hilar shadow and mediastinal extension in 10 months (Figs. 7, 8, and 9).

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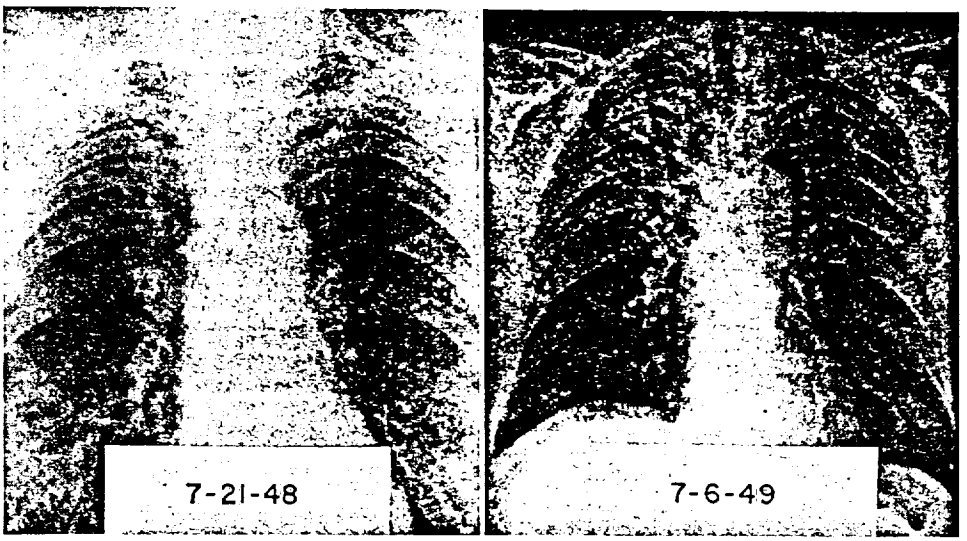

Fig. 10. Fig. 11.

Figs. 10-11.—R. W., SMH No. 298690. A 66-year-old man admitted July, 1949, with cough, hemoptysis, wheeze, and a 20-pound weight loss during the preceding 2 months. Chest x-ray studies a year before admission (Fig. 10) revealed an ill-defined, round density at the upper right hilum. A year later this had enlarged with a considerable component of atelectasis of the right upper lobe as indicated by the elevated hilum and diaphram (Fig. 11). Biopsy of a cervical lymph node revealed anaplastic carcinoma. Patient died one month following a course of palliative radiation therapy.

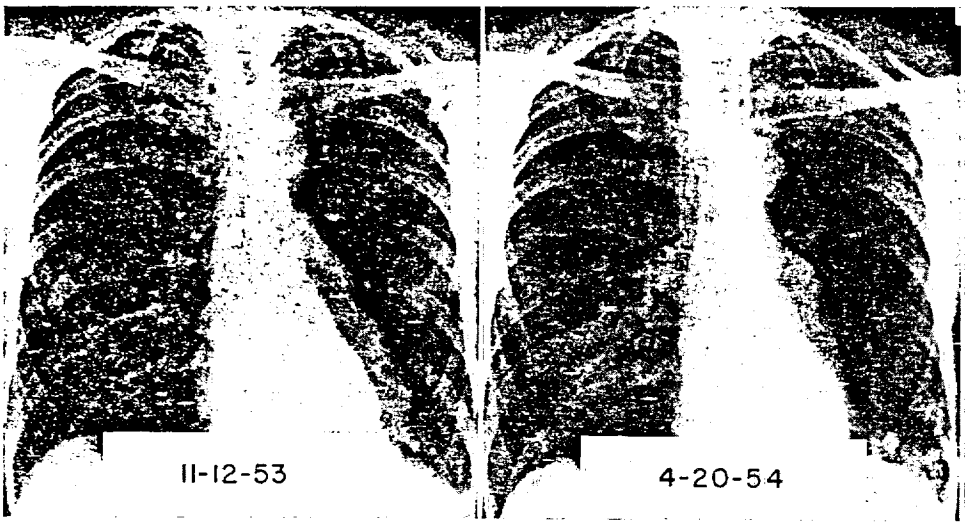

Fig. 12. Fig. 13.

Figs. 12-13.—M. Mc., SMH No. 181748. A 65-year-old counterman admitted in November, 1954, with increasing cough during the preceding 2 years and a 35-pound weight loss. He had had negative chest films until 11/23/53 (Fig. 12), when an interpretation of thoracic aortic aneurysm was made. The dense shadow along the left heart border is actually an atelectatic left lower lobe with the outline of the heart border seen through it. Five months later (Fig. 13), further collapse is shown with associated emphysema of the left upper lobe. Biopsy at bronchoscopy revealed epidermoid carcinoma and thoratomy proved the lesion to be inoperable. Patient died 9 months later.

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smaller, more significant group, plays a prominent part in the delayed diagnosis of pulmonary cancer. If we are to improve the cure rate, all methods to shorten this interval must be used.

The data relating to the early radiographic findings in cancer of the lung have emphasized that certain changes are highly significant. Hilar, mediastinal and large parenchymal masses, as well as gross atelectasis, produce radiographic shadows strongly suggestive of carcinoma and are of serious prognostic import. Somewhat less obviously produced by a cancer but to be viewed with a high degree of suspicion are obstructive pneumonitis, the small hilar nodule, localized emphysema, and thick-walled irregular abscesses. These carry a slightly less grave outlook, when diagnosed without delay.

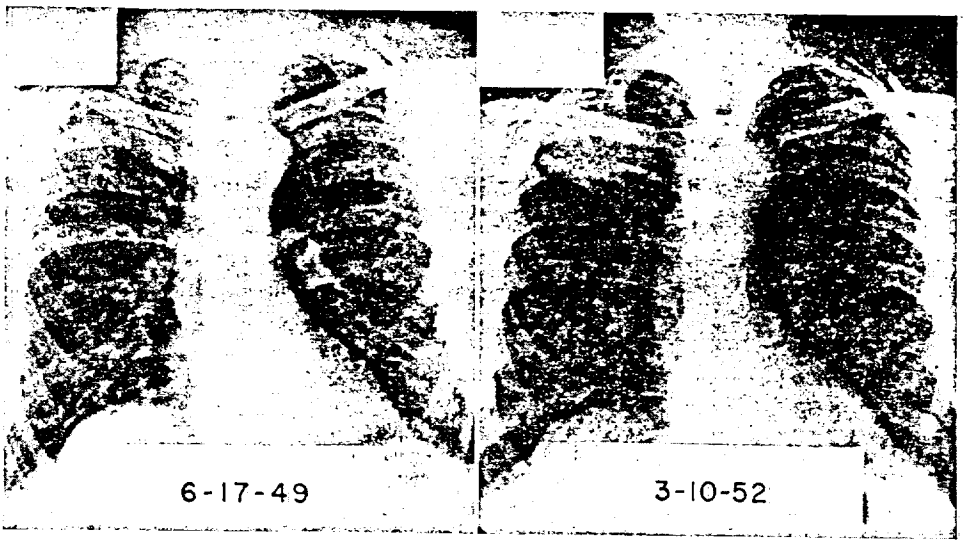

Fig. 14. Fig. 15.

Figs. 14-15.—J. W., SMH No. 295160. A 58-year-old male reporter admitted in March, 1952, with fatigue, cough, and upper chest pressure. Admission chest film (Fig. 15) revealed a large right apical mass and review of a film taken 2½ years previously (Fig. 14) showed a faint fibrous infiltrate in the first right anterior interspace. At thoracotomy, the lesion was proved to be inoperable and biopsy revealed adenocarcinoma. Patient died 6 months later.

Much has been written recently about the isolated parenchymal nodule which the authors feel is malignant until proved otherwise.[6] As indicated above (Table XI), the smaller the nodule, the less apt it is to have other associated radiographic changes and the better is its prognosis. It is felt that the small persistent infiltrative density should be viewed with almost as much suspicion as the isolated nodule. It will most frequently be confused with a residual fibrous change from inflammatory disease and the distinction, on pure radiographic grounds, is often impossible with a single film. As in the study of changes in the hilar region, the review of current films with any other previous films is of great aid in evaluating the parenchymal nodule and infiltrative density. Even if there are no clues to the radiographic differentiation, the persistent parenchymal infiltrate warrants close follow-up and thorough clinical evaluation. The increase in number of resections now being done for these lesions should yield a better 5-year survival.

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A definite factor in late diagnosis of carcinoma of the lung is the abnormal film which is read as normal. This will happen with even the most experienced eye and will not be completely eliminated. However, all efforts can be constructively directed toward keeping this factor to a minimum. In the case of mass survey examinations, it is frequently not trained radiologists or chest specialists who interpret the films but other physicians, equally loath to miss a diagnosis but without the specialists' experience. In such cases, and even in the established x-ray department, the ideal would include double reading of films, particularly the normal films.

A very minimal change in the hilar shadow is frequently overlooked on a single film where it would be more obvious when compared with a previous normal film. Consequently, when a patient is being studied for possible chest disease, every effort should be made to gather all available past roentgenograms for combined study by the clinician and radiologist. In this regard, the destruction of chest films should be discouraged.

As indicated by Table IX, some 44 per cent of the patients in this series had no film taken prior to the time of diagnosis, or none was available. Yet, the changes present on admission films were such that many patients would have had positive radiographs if films had been taken during the preceding year. An increase in the frequency of films should, therefore, provide earlier case findings. In order to increase the number of chest films taken, the general increase in mass surveys in people over 40 years of age must be supported and patients must be encouraged to obtain periodic x-ray studies of the chest along with physical examinations. Where practical, the individual should be encouraged to have routine x-ray studies done at the same radiologic unit for better comparison follow-up.

Confronted with a suspicious shadow on a chest film and a consequent suspicious lesion in the thorax, it is mandatory that there be continuity of observation and patient care. Increasing numbers of patients suspected of a cancer of the lung today are given the advantage of modern methods of diagnosis. Where the working diagnosis of pulmonary cancer is made more promptly on first recognizing abnormal x-ray shadows, these diagnostic methods will be employed earlier in the course of the disease. It should be emphasized that a high index of suspicion will necessarily make more diagnoses than there are cases and one cannot presume that all suspicious lesions will turn out to be cancer. However, unless one presumes that they might, the toll of bronchogenic carcinoma will not be significantly reduced.

SUMMARY

This paper is a study of 360 cases of proved bronchogenic carcinoma with particular reference to the radiographic appearance of such lesions on any past radiographs before definitive diagnosis. Statistical information has been accumulated for general interest.

The average interval of time between early radiographic change and diagnosis for all patients was 4 months. In a selected group (considered more

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significant) in which radiographs were available more than 6 months before diagnosis, this interval reached the alarming figure of almost 16 months.

The types of early radiographic changes are described. Methods of reducing the time interval between radiographic change and diagnosis and, thus, improving the current low cure rate, are discussed.

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